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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,387	03/26/2001	Eckart Matthes	101195-24	9650
27387	7590	03/31/2005	EXAMINER	
NORRIS, MCLAUGHLIN & MARCUS, P.A. 875 THIRD AVE 18TH FLOOR NEW YORK, NY 10022			EPPS FORD, JANET L	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/817,387

Applicant(s)

MATTHES ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 3 and 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1, 2 and 5-17 is/are allowed.
- 6) ☒ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/423,157.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3-26-01</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

2. In response to the Election/Restriction requirement mailed 1/29/03, Applicants elected group 1 (See response filed 4/01/03), drawn to chimeric oligonucleotides having a phosphorous containing backbone, and further elected SEQ ID NO: 16. It is noted that the Election/Restriction mailed 1/29/03 improperly included claims 3-4 in group I, the invention according to group I was defined as chimeric oligonucleotides comprising a phosphorous backbone, however these claims are drawn to chimeric oligonucleotides comprising a polyamide backbone. Additionally, claim 2 should not have been included in group II, claim 1 is drawn chimeric oligonucleotide containing a phosphorous backbone, however group II is drawn to chimeric oligonucleotides comprising a polyamide backbone.

3. Therefore, claims 3-4 should have been withdrawn from consideration by the examiner as being directed to non-elected subject matter. Additionally, new claims 13-16 recite SEQ ID NO: 1-28. Applicants are reminded that SEQ ID NO: 16 was elected by Applicants in the response filed 4/01/03. SEQ ID NO: 2-28 are not considered as part of the elected invention and were not searched by the examiner.

Response to Amendment

4. Applicant's markings in claim 1 with regards to the "=" symbols are confusing. It is unclear if Applicants are adding these symbols or deleting them. If Applicants are intending on deleting these symbols, Applicants should use "[]" instead of a strike through. Additionally, in

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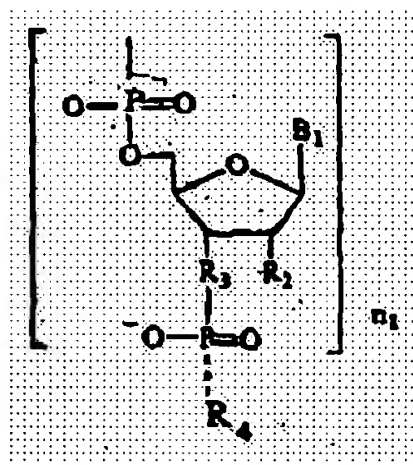
the Amendment filed 8/12/04, Applicants added the phrase "p is at least 3 and not more than 17," to claim 1, however there are markings in the response filed 12/06/04 that also indicate that this phrase was added to claim 1.

Claim Rejections - 35 USC § 112

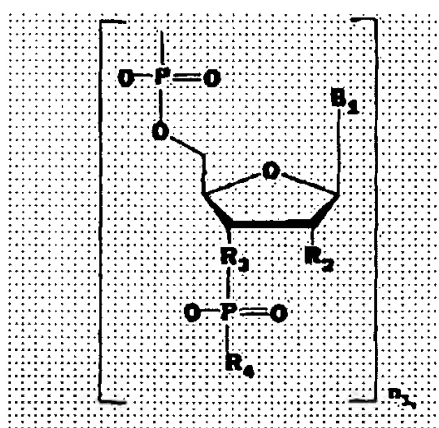
5. Claims 1-2, and 5-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter).

6. In the response filed 7/16/03 Applicants amended the structure of the "R" groups such that the definition of the repeating unit n_1 in each structure corresponding to "R" is different from what Applicants defined the repeating units to be in the claims and specification as originally filed. For example:

The original claim recited wherein R is defined as:



In the amendment filed 7/16/2003, Applicants amended claim 1 by replacing the above structure with the following:



The amendment filed 7/16/2003 did not include any markings to indicate this change in the definition of the repeating unit n_1 . Additionally, Applicants removed the charge on one of the terminal oxygen atoms ($O^- \rightarrow O$), and have replaced the dashed bond between $P---R_4$ with a solid line $P—R_4$. Neither the specification as filed nor the claims provide adequate support, either expressly or implicitly, for Applicant's amendment. Moreover, Applicant's response filed 7/16/2003 does not mention the above amendment to the definition of the repeating units of the "R" groups. Applicant's amendment is considered to introduce new matter into the claims, since Applicant's amendment is not supported by the original disclosure. Applicant is required to cancel the new matter in the reply to this Office Action.

Election/Restrictions

7. In response to the Election/Restriction requirement mailed 1/29/03, Applicants elected group 1 (See response filed 4/01/03), drawn to chimeric oligonucleotides having a phosphorous containing backbone, and further elected SEQ ID NO: 16. It is noted that the Election/Restriction mailed 1/29/03 improperly included claims 3-4 in group I, the invention according to group I was defined as chimeric oligonucleotides comprising a phosphorous backbone, however these claims are drawn to chimeric oligonucleotides comprising a polyamide backbone. Additionally, claim 2 should not have been included in group II, claim 1 is drawn chimeric oligonucleotide containing a phosphorous backbone, however group II is drawn to chimeric oligonucleotides comprising a polyamide backbone.

8. Therefore, claims 3-4 should have been withdrawn from consideration by the examiner as being directed to non-elected subject matter. Additionally, new claims 13-16 recite SEQ ID NO: 1-28. Applicants are reminded that SEQ ID NO: 16 was elected by Applicants in the response

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filed 4/01/03. SEQ ID NO: 2-28 are not considered as part of the elected invention and were not searched by the examiner.

Response to Arguments

Claim Rejections - 35 USC § 112

9. Claims 8, and 12-16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using chimeric oligonucleotides according to the present invention to inhibit telomerase activity *in vitro* comprising the administration of chimeric oligonucleotides, and provides guidance for inhibiting telomerase activity in human cancer cells transplanted into a nude mouse, does not reasonably provide enablement for using chimeric oligonucleotides of undefined structure and/or target, *in vivo* for treating cancer in all non-human mammals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

10. Applicant's arguments filed 2-17-04 have been fully considered but they are not persuasive. Applicants traversed the instant rejection by way of amending claim 7 to refer back to the oligonucleotide structure in claim 1, and further have amended claim 8 to replace the term *treat* with *inhibiting the telomerase activity* of the tumor cell *in vivo*. According to Applicants they have addressed the Examiner's concerns by "relating to [a] the structure of the oligos and [b] the preamble reciting 'treatment' have been addressed by amendment."

Contrary to Applicant's assertions, Applicants have not fully addressed the scope of enablement rejection of claims 7-8 set forth in the Office Action mailed 11-17-2003. Although Applicants have amended claim 7 to refer back to the structure of the oligonucleotide described

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in claim 1, this amendment does not provide evidence of enablement for the full scope of the instant claims. In the prior Office Action, the examiner has previously stated that the instant claims are enabled for practicing the claimed method *in vitro* using the oligonucleotides according to SEQ ID NO: 1-28. However, Applicants have not addressed the issues raised in the prior Office Action. Specifically, Applicants have not provided any evidence that the skilled artisan would be able to practice the full scope of the claimed invention without undue experimentation. In particular, Applicants have not provided sufficient guidance and/or instruction that would allow the skilled artisan to use the oligonucleotide compounds according to the present invention in a method for the treatment of conditions associated with telomerase activity, for example cancer, in any non-human animal, other than in transplanted human cells in a nude mouse.

As stated in the prior Office Action, Chirila et al. (2002), Jen et al. (2000), and Stein (2000) teach that the behavior of oligonucleotide based compositions and their delivery *in vivo* are unpredictable, therefore claims to pharmaceutical compositions and methods of treating diseases by the administration of oligonucleotide based pharmaceuticals are subject to the question of enablement due to the high level of unpredictability associated with this technique as taught in the prior art. It was also previously stated that the quantity of experimentation required to practice the invention as claimed would require determining modes of delivery in a whole organism such that an undefined target nucleic acid is inhibited and the desired secondary effect of treating tumors is obtained. The specification as filed provides no specific guidelines in this regard; the specification merely provides a prophetic example for using the claimed compositions *in vivo*. The deficiencies in the specification would constitute undue

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experimentation since these steps must be achieved without instruction from the specification before one is enabled to practice the claimed invention. Applicants have not provided any arguments to address these issues as set forth in the prior Office Action.

Applicant's response does not fully address the issues raised in the prior Office Action, therefore, it remains that the specification as filed does not teach the skilled artisan how to use the chimeric oligonucleotides of undefined nucleobase composition, according to the present invention for inhibiting telomerase activity *in vitro* or *in vivo* treatment purposes, without undue experimentation. This conclusion is based upon the known unpredictability regarding the behaviour of oligonucleotide compositions in a cell, delivery of antisense *in vivo*, irrelevant cleavage of non-specific targets, the quantity of experimentation required to practice the full scope of the claimed invention (which reads on the therapeutic use of the claimed pharmaceutical composition) and the lack of guidance thereof in the specification as filed in this regard.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

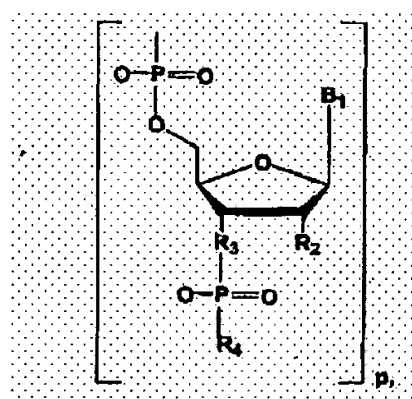
12. Claims 1-2, remain rejected and claims 5, 9-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Uhlmann et al. for the reasons of record set forth Office Action mailed 11-17-03.

13. Due to the uncertainty in regards to the structure of the compounds according to general formula I recited in the instant claims (in regards to the definition of the repeating unit n_1), and

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further with the uncertainty associated with the nucleotide structure of the chimeric oligonucleotides according to the present invention, the prior art is applied to the extent that the prior art is applied to the extent that the overall length of the oligonucleotide is at least 10 nucleotides in length, and the repeating structure n_1 in the definition of "R" (corresponding to the phosphorous backbone containing moiety) recited in claim 1 does not include R_4 .

14. Applicant's arguments filed 2-19-04 have been fully considered but they are not persuasive. Applicants traverse the instant rejection the grounds the DNA/PNA compounds of Uhlmann et al. do not comprise the requisite number of n and p repeats as recited in the instant claims. However, contrary to Applicant's assertions it is noted that the instant claims encompass wherein the full length oligonucleotide is an DNA molecule particularly wherein R is:



and wherein R_3 is O, and R_4 is 2'-deoxyguanosine, 2'-deoxyadenosine, 2'-deoxycytosine, or 2'-deoxythymidine. Absent evidence to the contrary, since the compounds of Uhlmann et al. are at least 10 nucleotides and not more than 20 nucleotides in length, the compounds of Uhlmann et al. encompasses the requisite number of n and p repeats as set forth in the structure of the chimeric oligonucleotides recited in the instant claims. Moreover, since the compounds recited in Uhlmann et al. meet the structural limitations of the instant claims, absent evidence to the contrary, the compounds of Uhlmann et al. would also possess the functional characteristics of

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the compounds of the claimed invention. See MPEP § 2112[R-2]III. Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103.

Specification

15. The disclosure is objected to because of the following informalities: There are multiple instances of misspelled text. For example: see page 1, 4th paragraph, the term “tyrosinekinase” likely should have been spelled “tyrosine kinase;” the term “oncognes,” should be spelled “oncogenes.” Page 2, 1st and 4th paragraphs, the term “telemeric,” should have been spelled “telomeric.” Page 3, 3rd paragraph, the term “telomerase” should have been spelled “telomerase.” Page 4, 1st paragraph, the term “linger” should have been spelled “longer;” 2nd paragraph the term “tighty” should be “tightly.” There are several other instances of misspelled words in the specification as filed. Applicants are request to review the contents of the specification again, and confirm the appropriate spelling of each word.

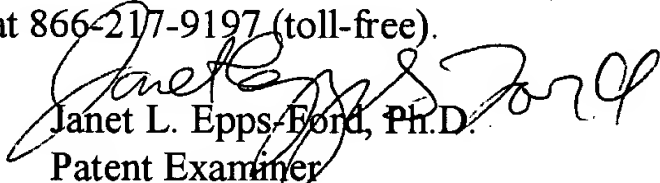
Appropriate correction is required.

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16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Janet L. Epps-Ford, Ph.D.
Patent Examiner
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